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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,966	04/20/2005	Carl T Wittwer	P00950-US-01	8958

7590 09/12/2008

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EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
09/12/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,966	WITTWER ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,18-20,23-30,33-35,37,39,40,43,45-51,53-58,61,65 and 66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,18-20,23-30,33-35,37,39,40,43,45-51,53-58,61,65 and 66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 April 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' response to the office action filed on March 18, 2008 has been considered and acknowledged.

Status of the Application

2. Claims 2-3, 18-20, 23-30, 33-35, 37, 39-40, 43, 45-51, 53, 55-58, 61, 65-66 are considered for examination in this office action. Claims 1, 4-17, 21-22, 31-32, 36, 38, 41-42, 44, 52, 54, 59-60, 62-64 are cancelled. Applicants' response to the office action is fully considered. All arguments have been fully considered and thoroughly reviewed and are deemed persuasive in-part for the reasons that follow.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 2, 20, 23-28, 33-35, 37, 49-40, 43, 45-48 are rejected under 35 U.S.C. 102(a) as being anticipated by Elenitoba-Johnson (US 6,346,386).

Elenitoba-Johnson teaches a method of claim 24-25, 45-46, of PCR analysis comprising providing a mixture of a target nucleic acid, PCR reagents, oligonucleotide primers configured for amplifying the target nucleic acid and a dsDNA binding dye having percent saturation of at least 50% or at least 80% (YO-PRO-1), amplifying nucleic acid in the presence of the dye and monitoring the amplified nucleic acid by generating the melting curves from the amplified target

nucleic acid using fluorimeter, normalizing the melting curve, repeating the providing amplifying normalizing and generating steps with at least one additional target nucleic acid and comparing the normalized melting curves and plotting the fluorescence difference between the normalized curves superimposing a portion of the curve and plotting the fluorescence difference between the curves (see col. 3, line 6-67, col. 4, line 1-67, col. 5, line 1-5, col. 6, line 35-54).

With regard to claim20, 23, Elenitoba-Johnson teaches that the target nucleic acid comprises single nucleotide polymorphism and the method comprises mutational scanning and identifies resultant hetero and homoduplexes (see col. 3, line 6-67, col. 4, line 1-67, col. 5, line 1-5, col. 6, line 35-54).

With regard to claim 26-28, 47-48, Elenitoba-Johnson teaches that the method comprises the step of plotting the fluorescence difference between normalized curves, and plotting temperature shifted curves (see col. 3, line 41-50, col. 4, line 57-67, col. 5, line 1-5, col. 7, line 18-30).

With regard to claims 37, 39-40, 43, Elenitoba-Johnson teaches that the target nucleic acid comprises two melting domains and the method comprises repeating mixing, amplifying and melting steps with one additional target nucleic acid, comparing the melting curve for the target nucleic acid with the melting curve for the additional target nucleic acid (see col. 3, line 6-50, line 62-67, col. 4, line 1-44). Accordingly Elenitoba-Johnson anticipates the instant claims.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject

matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

A. Claims 3, 18-19, 29-30, 33-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elenitoba-Johnson (US 6,346,386) in view of Erikson et al (US 6,927,027).

Elenitoba-Johnson teaches a method of PCR analysis as discussed above in section 3. However Elenitoba-Johnson specifically did not teach saturating dyes as claimed in claims 29-30, excitation and emission maximum in a range of 410-465nm and 450-500 nm.

Erikson et al. teach a method for nucleic acid multiplex formation wherein the method comprises the use of DNA binding intercalator dyes as accelerator agents, that are selected from the group consisting of PO-PRO-1, JO-PRO-1, SYTOX, SYTO dyes, LO-PRO-1, BOBO-3, YOYO-3, BO-PRO-1, TOTO-3. TO-PRO-1 (see col. 7, line 14-30). Erikson et al. also teach use of a probe in said method (see col. 3, line 46-61, col. 11, line 41-48) and the excitation and emission wavelength of the dyes ranging from 200 to 1000nm (see col. 11, line 49-51).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of monitoring amplification of a target nucleic

acid during PCR in the presence of a dsDNA binding dye as taught by Elenitoba-Johnson with a step of including accelerator agents that enhance the specificity of the signal detection as taught by Erikson et al. for the purpose of developing an improved real-time amplification method. One skilled in the art would be motivated to combine the references because an ordinary artisan skilled in the art would have a reasonable expectation of success that the method would result in enhancing the specificity because Erikson et al. explicitly taught the use of the intercalating agents as accelerators that enhance the specificity of probe-target binding and the signal generated by the intercalating agents is directly correlated to the probe-target binding thereby increasing the extent of matching between probe and the target (see col. 16, line 47-63) and such modification of the method would be obvious over the cited prior art.

B. Claims 65-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elenitoba-Johnson (US 6,346,386) in view of Nurmi et al (Anal. Biochem., Vol. 299, pp. 211-217, December, 2001).

Elenitoba-Johnson teaches a method of PCR analysis as discussed above in section 3. However Elenitoba-Johnson specifically did not teach target nucleic acid as a locus of HLA gene.

Nurmi et al. reach a PCR analysis in the presence of a ds binding dye and a probe wherein the method comprises a target nucleic acid comprising HLA gene (see page 213, col. 1, paragraph 1 under all-in-one dry reagent concept, page 215, col. 1, line 2-27, col. 2, paragraph 2).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of monitoring amplification of a target nucleic acid

during PCR in the presence of a dsDNA binding dye as taught by Elenitoba-Johnson with a step of including a highly polymorphic HLA gene as a target nucleic acid as taught by Nurmi et al. for the purpose of detecting single nucleotide polymorphisms. One skilled in the art would be motivated to combine the method as disclosed by Elenitoba-Johnson with target HLA gene as taught by Nurmi et al. because Nurmi et al. explicitly taught the real-time monitoring of HLA gene target in the presence of a dsDNA binding dye would eliminate false positives and since detection of SNPs is very useful in linkage and disease marker association studies, the method provides highthrouput analysis of SNPs (see page 215, col. 1, line 2-27, col. 2, paragraph 2). The ordinary artisan would have had a reasonable expectation of success that inclusion of inclusion of said target would result in a high throughput analysis of highly polymorphic loci such as HLA gene as suggested by Nurmi et al. and such modification of the method would be obvious over the cited prior art.

Non-Statutory Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225

USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 24, 49-50, 53, 55-58, 61 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2 of U.S. Patent No. 7,387,887 ('887). An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed.Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed.Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims 24, 49-50, 53, 55-58, 61 are generic to all that is recited in claims 1-2 of the patent '887. That is, the claims 1-2 of the patent '887 fall entirely within the scope of claims 24, 49-50, 53, 55-58, 61 or in other words, claims 24, 49-50, 53, 55-58, 61 are anticipated by the claims 1-2 of the patent '887. Thus the instant claims encompass the claims in the patent ('887) and are related as genus and species, and are coextensive in scope.

The courts have stated that a genus is obvious in view of the teachings of a species. see Slayter, 276 F.2d 408, 411, 125 USPQ 345, 347 (CCPA 1960); and In re Gosteli, 872 F.2d 1008, 10 USPQ2d 1614 (Fed.Cir. 1989). Therefore the instantly claimed method is obvious over the claims in the patent. Thus the instant claims are rejected under obviousness-type of double patenting.

Response to arguments:

6. With regard to the rejection of claims 49-51, 53, 55-58 under 35 USC 112, second paragraph, Applicants' arguments were found unpersuasive. MPEP 2145 states Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993), Accordingly the specification can not be read into the claims and the limitations upon which the arguments were based, are not present in the instant claims. Accordingly the rejection is maintained.

7. All the rejections under 35 USC 102 and 103(a) that are not reiterated herein are withdrawn in view of the Applicants' arguments and the amendment.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Suryaprabha Chunduru/

Primary Examiner, Art Unit 1637